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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/029,653

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Laura A. Browning

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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/029,653

Applicant(s)

BROWNING, LAURA A.

Examiner

David J Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 19-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 19-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>03/29/02</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

- [1] Claims 1-10 and 19-24 are pending in the application.
- [2] Applicant's amendment to the claims, filed June 09, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

Election/Restriction

- [3] Applicant's election without traverse of the invention of Group I, claims 1-10 and 19-24, filed June 09, 2004, is acknowledged.

Priority

- [4] Applicants' claim to domestic priority under 35 USC 119(e) to US provisional application 60/256,586, filed December 19, 2000, is acknowledged.

Oath/Declaration

- [5] As stated in a previous Office action, the Declaration claims priority under 35 USC 119(e) to non-provisional US application 09/256,586, filed December 19, 2001. This information is inconsistent with applicant's claim for domestic priority under 35 USC 119(e) as stated at the first paragraph of the specification. It is suggested that applicants correct the discrepancy.

Information Disclosure Statement

[6] All references cited in the IDS filed March 29, 2002 have been considered by the examiner. A copy of Form PTO-1449 is attached to the instant Office action.

Specification/Informalities

[7] The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification (for example, page 9, line 7, page 23, line 27) is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference.

[8] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: -- Human Double-Stranded RNA Dependent Protein Kinase-Overexpressing Cells --.

Claim Objections

[9] Claims 1-3, 8, 10, 19-20, and 23 are objected to in the recitation of "PKR." Abbreviations, unless otherwise obvious, e.g., the recitation of "DNA" for deoxyribonucleic acid, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. Appropriate correction is required.

[10] Claims 2-3 and 19 appear to be grammatically incorrect in the recitation of "wherein the process further comprising" (claim 2), "wherein said preparative process further comprising" (claims 3 and 20), "enhanced cytokines production" and should be

replaced with, for example, "wherein the process further comprises," "wherein said preparative process further comprises," "enhanced cytokine production," respectively.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[11] Claim(s) 2-3, 5-10, and 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 2-3, 5-10, and 19-24 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. It is noted that the claims are limited to cells that characterized by enhanced production of one or more cytokines. From the specification, it would appear that a cell expressing enzymatically active PKR is required for the enhanced production of cytokines, however, the claims are not so limited. While it is acknowledged that the cells express an increased level of PKR, this is no indication that the PKR has enzymatic activity.

[b] Claims 2 (claim 3 dependent therefrom) and 20 are indefinite in the recitation of "priming." It is unclear from the claims and the specification as to specifically how the cells are primed and what is used for the priming. It is suggested that applicants clarify the meaning of the claims.

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[c] Claims 3 and 20 are indefinite in the recitation of "treating." It is unclear from the claims and the specification as to how the cells are treated and what is used for this treatment. It is suggested that applicants clarify the meaning of the claims.

[d] Claim 10 is indefinite in the recitation of "treated and induced in a manner effective to result in enhanced PKR and cytokine production." It is unclear from the claims and the specification as to the effective manner of treating and inducing cells that will achieve enhanced PKR and cytokine production. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[12] Claims 1-10 and 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to PKR-overexpressing cells prepared by limiting dilution or transfection with a PKR expression vector. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a genus may be satisfied through

sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only two representative species of the genus of claimed PKR-overexpressing cells prepared by limiting dilution, i.e., Namalwa cell lines 41.027.A9 and 41.027.C1 prepared by the method of Example 1 of the specification and the specification discloses only a single representative species of the genus of claimed PKR-overexpressing cells prepared by transfection, i.e., a human cell line transfected with an expression vector encoding human p68 PKR having GenBank Accession Number M35663 (page 19 of the specification). Other than these species, the specification fails to disclose other species that are encompassed within the genus of claimed PKR-overexpressing cells. In this case, the specification encompasses species that are widely variant with respect to the cell and PKR that is overexpressed. Given the lack of description of a representative number of compounds, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms

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that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[13] Claim(s) 1-10 and 19-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Namalwa cell lines 41.027.A9 and 41.027.C1 prepared by the method of Example 1 of the specification and a human cell line transfected with an expression vector encoding human p68 PKR having GenBank Accession Number M35663, does not reasonably provide enablement for all PKR-overexpressing cells prepared by limiting dilution cloning or transfection of a human cell line using a PKR expression vector as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP §

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2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass a vast number of PKR-overexpressing cells prepared by limiting dilution cloning or transfection of a human cell line using a PKR expression vector. It should be noted that the PKR's overexpressed by the human cells are not limited to those that are known in the art, but are intended to encompass mutants and variants thereof, including allelic variants (see, for example, page 19 of the instant specification), that have not been disclosed in the prior art. The broad scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the vast number of PKR-overexpressing cells broadly encompassed by the claims. In this case the disclosure is limited to Namalwa cell lines 41.027.A9 and 41.027.C1 prepared by the method of Example 1 of the specification and a human cell line transfected with an expression vector encoding human p68 PKR having GenBank Accesssion Number M35663.
- The lack of guidance and working examples: The specification provides only two working examples of human PKR-overexpressing cells prepared by limited dilution cloning, i.e., Namalwa cell lines 41.027.A9 and 41.027.C1 prepared by the method of Example 1 of the specification. The specification provides no further guidance regarding the use of other human cells that can be obtained by limiting dilution cloning to obtain cells having the desired biological characteristics. Also, the specification provides only a single working example of human PKR-overexpressing cells prepared by transfecting a human cell with a PKR expression vector, i.e., a human cell line transfected with an

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expression vector encoding human p68 PKR having GenBank Accession Number M35663.

- The high level of unpredictability in the art: Regarding the human PKR-overexpressing cell line prepared by limited dilution cloning, it is noted that, while applicants present two working examples, of the claimed cells, there is a high level of unpredictability in using other cell lines to achieve similar results. Moreover, even if other cell lines could be used to obtain the human PKR-overexpressing cells, it is noted that there is a high level of unpredictability in obtaining a human PKR-overexpressing cell by using altered conditions from those presented in Example 1. Regarding the human PKR-overexpressing cell line prepared by transfection, it is noted that, while such methods are known in the art, there is a high level of unpredictability in altering the encoding sequence for a given polypeptide with an expectation of obtaining a polypeptide having the desired characteristics. See Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991, page 247) and Witkowski et al. (*Biochemistry* 38:11643-11650, particularly Table 1, page 11647).
- The amount of experimentation required: It is not routine in the art to screen all human cell lines for those that can overexpress PKR. Further, it is not routine in the art to screen all polynucleotides, including mutants and variants thereof, for those that encode a catalytically active polypeptide.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high degree of unpredictability, and

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the significant amount of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. As such, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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[14] Claim(s) 1-10 and 19-24 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by Lau et al. (US Patent 6,159,712). The claims are drawn to human cell compositions comprising PKR-overexpressing cells, wherein said cells overexpress PKR at a level at least 2-fold greater than a parental cell. Lau et al. teach the preparation of human U937 cells overexpressing PKR (columns 6-8) by transfecting the U937 cells with expression vectors encoding PKR downstream from a constitutively active or inducible promoter. This anticipates claims 1-10 and 19-24 as written.

[15] Claim(s) 1-10 and 19-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Yeung et al. (J Biol Chem 273:25198-25202). The claims are drawn to human cell compositions comprising PKR-overexpressing cells, wherein said cells overexpress PKR at a level at least 2-fold greater than a parental cell. Yeung et al. teach the preparation of human U937 cells overexpressing PKR (page 25199, middle) by transfecting the U937 cells with an expression vector encoding PKR downstream from a constitutively active promoter. This anticipates claims 1-10 and 19-24 as written.

[16] If applicant should traverse the instant rejection on the grounds that the PKR-overexpressing cells of Lau or Yeung et al. are not made by the same process as recited in the claims, applicants' attention is directed to MPEP 2113. Citing In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), MPEP 2113 states "[e]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is

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unpatentable even though the prior product was made by a different process.” MPEP 2113, citing In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983), further states, “[o]nce the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product.” Since the Office does not have the facilities for examining and comparing applicants’ claimed human cell composition comprising PKR-overexpressing cells with the PKR-overexpressing cells of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the PKR-overexpressing cells of the prior art do not possess the same material structural and functional characteristics of the claimed human cell composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Conclusion

[17] Status of the claims:

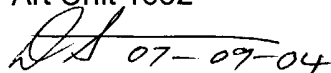
- Claims 1-10 and 19-24 are pending.
- Claims 1-10 and 19-24 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's

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supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 872-9306. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.
Patent Examiner
Art Unit 1652

 07-09-04